S.M.

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,721	12/14/2001	Jeanette McCarthy	MMI-003	5317

959 7590 03/15/2004

LAHIVE & COCKFIELD, LLP.
28 STATE STREET
BOSTON, MA 02109

EXAMINER	
SMITH, CAROLYN L	
ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,721	MCCARTHY ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 August 2003 and 30 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-134* is/are pending in the application.

4a) Of the above claim(s) *1-7,13-39 and 44-134* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-12 and 40-43* is/are rejected.

7)☒ Claim(s) *8-12 and 40-43* is/are objected to.

8)☒ Claim(s) *1-134* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12042003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of Group II (claims 8-12, 40-43, and 49-62) and election with traverse of SEQ ID NO: 1 and set of nucleotide positions 55322, 53502, 60793, 58445, 52861, and 49556, filed 12/30/03, and election with traverse of species L (a vascular imagining device which is angiography), W (a vascular disease which is coronary artery disease), and MM (a method of diagnosis of increased likelihood of disease), filed 8/19/2003, are acknowledged. Applicants misstated Group II as being claims 8-*21*, 40-43, and 49-62 in their election response. Group II is actually claims 8-*12*, 40-43, and 49-62, as stated on the first line of this Office Action. Claims 1-7, 13-39, 44-48, and 63-134 are withdrawn from consideration as being drawn to non-elected Groups. Claims 49-62 are withdrawn as being drawn to non-elected species (the entire elected set of nucleotide positions is not found in these claims).

Applicants' traversal is on the grounds that the requirement to elect a single nucleotide sequence does not encompass the entire invention that can include individual or both SEQ ID NO: 1 and 3. Applicants' submit that a search of SEQ ID NO: 1 and 3 would not present an undue burden to the Examiner. The traversal set for by Applicants is found unpersuasive for the following reasons:

The request for multiple sequences searched is found unpersuasive. Due to the number of these sequence requests made by Applicants in the field of biotechnology, it is practically impossible to accommodate all of these requests. The overwhelming number of sequences poses undue search burden when more than one nucleic acid sequence is elected.

The requirements are still deemed proper and are therefore made FINAL.

The information disclosure statement, filed 12/4/03, has been considered by the Examiner.

Claims herein under examination are 8-12 and 40-43.

Claim Objections

Claims 8-12 and 40-43 are objected to due to the inclusion of subject matter which has been non-elected due to a restriction requirement and therefore withdrawn from consideration. The non-elected subject matter in claims 8-12 and 40-43 is summarized as follows: These claims contain additional sequences with cited nucleotide positions that are not elected subject matter, such as SEQ ID NO: 3 and THBS4. Removal of such non-elected subject matter is requested.

Claim 8 is objected to because of the following minor informality: Claim 8, last 2 lines, recites the phrase "or the complement thereof, or the complement thereof" which seems to be redundant. Appropriate correction is requested.

Claim Rejections – 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and

reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF ENABLEMENT

Claims 8-12 and 40-43 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

Applicants set forth six single nucleotide polymorphisms (SNPs) for thrombospondin 1 (THBS1), including one (G334u4 at nucleotide position 55322) which is a variant allele shown to be associated with increased risk for vascular disease (page 88, lines 6-7 of specification). The specification notes that all six SNPs in the THBS1 gene were found to be in linkage disequilibrium with each other and that five SNPs (nucleotide positions 53502, 60793, 58445, 52861, and 49556) can act as markers for G334u4 (page 88, first paragraph). Table 2 (page 88) notes that G334a16 (at nucleotide position 52861) and G334k2 (at nucleotide position 49556) are found in negative linkage disequilibrium meaning that subjects with these variant alleles are less likely to vascular disease. The methods in the instant invention are directed to a determination of

the identity of all six nucleotides in these SNP locations; however, it does not appear that one of skill in the art would know, for example in claim 8, which variant alleles need to be present or which combinations of these variant alleles are necessary in order for the identification of a subject who is a candidate for further diagnostic evaluation for a vascular disease or disorder. For example, if the variant allele for G334u4 (positive indicator of vascular disease) is present as well as the variant alleles of G334a16 and G334k2 (negative indicators of vascular disease which are SNPs with negative linkage disequilibrium with G334u4), does this provide a stronger case for having coronary artery disease or not? Due to the necessity of additional undue experimentation, the lack of guidance and working examples addressing this issue, the instant claims are rejected due to a lack of enablement.

LACK OF WRITTEN DESCRIPTION

Claims 8-12 and 40-43 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

The specification discloses SEQ ID NO: 1 which corresponds to nucleic acid sequence of thrombospondin 1 (THBS1). SEQ ID NO: 1 and its full complement meet the written description provisions of 35 U.S.C. 112, first paragraph. However, claims 8-12 and 40-43 are directed to encompass the various other types of complements of SEQ ID NO: 1 that do not meet the written description provision of 35 U.S.C. 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by these claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmacentical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 1 and its full length complement, but not the full breadth of the claims 8-12 and 40-43 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Claims Rejected Under 35 U.S.C. § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 8-12 and 40-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 40 is vague and indefinite due to the unclarity of citing an abbreviation, such as THSB1. Correction is suggested by amending in of the full name in parentheses. Claims 41-43 are also rejected due to their direct or indirect dependency from claim 40.

Claims 8 and 41 recite the phrase "the complement thereof" which is vague and indefinite. The claims do not adequately define the phrase which could mean the complementarity is 100% similarity and of the same length of the claimed sequence, or 90% similarity and only a fragment of the claimed sequence, or any other scenario. Appropriate definition of the degree of complementarity to the claimed sequence is required. Claims 9-12 are also rejected due to their direct or indirect dependency from claim 8.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 8, 2004

ARDIN H. MARSCHEL
PRIMARY EXAMINER
3/12/04